REMARKS

Acknowledgement is made of Claims 1-27 being under consideration during the present course of examination and Claims 28-40 being withdrawn from consideration as being directed to a non-elected invention. Applicants respectfully request that the Examiner reconsider the restriction requirement as a search for the invention defined by the elected claims would necessarily entail a search of the non-elected claims. Favorable consideration is respectfully solicited.

In order to expedite the prosecution of the present application, the claims under consideration have been amended in order to more particularly point out and distinctly claim the subject matter which Applicants regard as the invention. That is, Claims 1 and 23, and the claims dependent thereon, now require that the composition be in the form of an in situ gellable solution, suspension or a solution/suspension having ophthalmically compatible pH and osmolality and contain a carrageenan. Newly presented Claims 41-46 require that the selective COX-2 inhibitory drug have a low water solubility and be in the form of an aqueous suspension or solution/suspension having ophthalmically compatible pH and osmolality in which the selective COX-2 inhibitory drug is present predominantly in the form of nanoparticles. Newly presented Claims 42 and 44 require that the average particle size of the drug is about 500 to about 900 nm. No new matter has been added. It is respectfully submitted that the currently presented claims are patentably distinguishable over the prior art cited by the Examiner.

Claims 1-7 and 23-27 have been rejected under 35 USC 102(b) as being anticipated by WO 00/25771. Claims 8-22 have been rejected under 35 USC 103(a) as being unpatentable over WO 00/25771 in view of Davis et al and Mazuel et al. Applicants respectfully traverse these grounds of rejection and urge reconsideration in light of the following comments.

The presently claimed invention is directed to a pharmaceutical composition which is used in topically administering a selective COX-2 inhibitory drug to an eye. The composition contains the COX-2 inhibitory drug and at least one ophthalmically acceptable excipient ingredient that reduces the rate of removal of the composition from the eye by lacrimation such that the composition has an effective residence time in the eye of about 2 to about 24 hours. The present invention is also directed to a method of treating and/or preventing a COX-2 media disorder in an eye of a mammalian subject which involves administration of the above-discussed pharmaceutical composition. In one embodiment of the present invention, the composition is in the form of an in situ gellable solution, suspension or solution/suspension having ophthalmically compatible pH and osmolality and containing a carrageenan. In another embodiment of the present invention, the selective COX-2 inhibitory drug is in the form of an aqueous suspension or solution/suspension having ophthalmically compatible pH and osmolality in which the selective COX-2 inhibitory drug is present predominantly in the form of nanoparticles.

As discussed in the present specification, numerous compounds have recently been used in the treatment or prevention of specific cyclooxygenase-2 mediated disorders. However, these drugs typically have a low water solubility and are difficult to provide in an aqueous formulation that can be topically administered to an eye. Additionally, due to the removal from the eye of a topically applied composition by lacrimation, it is difficult to provide a selective COX-2 inhibitory drug composition that has a sufficient residence time in the eye for an extended effective treatment. The presently claimed invention has been arrived at in order to overcome these problems.

In one aspect of the present invention, the composition is provided in the form of an in situ gellable solution, suspension or solution/suspension having ophthalmically

compatible pH and osmolality and containing a carrageenan in order to stabilize the drug formulation and enable topical long term delivery of the drug in the eye. In the other embodiment of the present invention, the selective COX-2 inhibitory drug has a low water solubility, is in the form of an aqueous suspension or solution/suspension having ophthalmically compatible pH and osmolality and is present predominantly in the form of nanoparticles. This aspect of the present invention is based on the discovery that by providing a selective COX-2 inhibitory drug having low water solubility in the form of nanoparticles, the drug could be released in a significantly faster rate than from a typical "micronized" composition having a D_{90} particle size of, for example, about 10 microns or greater. Moreover, it was unexpectedly found that a selective COX-2 inhibitory drug composition having a weight average particle size of from about 450 to about 1,000 nm exhibited an onset time and bioavailability substantially equal to that of a comparative composition having a weight average particle size of from about 200 to about 400 nm. Since the 450 to about 1,000 nm particle size formulation requires less milling time and energy than a formulation comprising smaller nanoparticles, this is clearly an unexpected and advantageous aspect of the present invention. It is respectfully submitted that the prior art cited by the Examiner does not disclose the presently claimed invention.

WO 00/25771 discloses anti-inflammatory agents used to prevent iridial pigmentation during prostaglandin treatment. However, this reference has no disclosure with respect to the use of a carrageenan in the ophthalmic composition or the selective COX-2 inhibitory drug being provided in the form of nanoparticles, and the advantages associated therewith.

The Davis et al reference discloses ophthalmic suspensions containing lightly cross-linked polymers which provide topical ophthalmic medicament delivery systems having low viscosities which permit them to be easily administered to

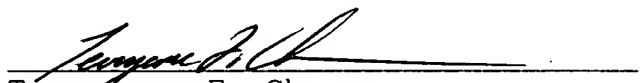
the eye in drop form and which rapidly gel in the eye after coming into contact with the eye's tear fluid and thereby remain in place for prolonged periods of time to provide sustained release of the ophthalmic medicament.

As with the Davis et al reference, Mazuel et al discloses ophthalmic compositions which undergo a liquid-gel phase transition when brought into contact with physiological liquids.

Neither of the secondary references cited by the Examiner, Davis et al and Mazuel et al, teach the use of carrageenan in the ophthalmic composition nor suggest the provision of the selective COX-2 inhibitor in the form of nanoparticles, and the unexpected benefits associated therewith. As such, it is respectfully submitted that the presently claimed invention clearly is patentably distinguishable over the cited references.

The Examiner is respectfully requested to reconsider the present application and to pass it to issue.

Respectfully submitted,



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